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Research Article

Preparation and Characterization of Emamectin Benzoate Solid Nanodispersion

Dongsheng Yang, Bo Cui, Chunxin Wang, Xiang Zhao, Zhanghua Zeng, Yan Wang, Changjiao Sun, Guoqiang Liu, and Haixin Cui

Institute of Environment and Sustainable Development in Agriculture, Chinese Academy of Agricultural Sciences, Beijing 100081, China

Correspondence should be addressed to Haixin Cui; cuihaixin@caas.cn

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The solid nanodispersion of 15% emamectin benzoate was prepared by the method of solidifying nanoemulsion. The mean particle size and polydispersity index of the solid nanodispersions were 96.6 ± 1.7 nm and 0.352 ± 0.041, respectively. The high zeta potential value of 31.3 ± 0.5 mV and stable crystalline state of the nanoparticles suggested the excellent physical and chemical stabilities. The contact angle and retention compared with microemulsions and water dispersible granules on rice, cabbage, and cucumber leaves indicated its improved wettability and adhesion properties. The bioassay compared with microemulsions and water dispersible granules against diamondback moths and green peach aphids provided an evidence of its enhanced biological activity. This formulation composition could avoid organic solvents and obviously reduce surfactants. It is perspective in raising bioavailability and reducing residual pollution of pesticides and further improving agricultural production and environmental safety.

1. Introduction

In conventional agroecological systems, pesticides are primarily used to control pests, diseases, and weeds in order to ameliorate the yield and quality of crop products [1, 2]. However, most of pesticide compounds are generally poorly soluble in water which is not benefit to maintain bioactivity and increase efficacy and safety of the active ingredients after spraying [3]. The conventional pesticide formulations generally involve emulsifiable concentrate (EC), microemulsion (ME), suspension concentrate (SC), wettable powder (WP), and water dispersible granule (WDG) [4, 5]. These formulations have several disadvantages, such as poor dispersion in water, dust drift in atmosphere, and organic solvent pollution in ecosystem, consequently, decreasing the control efficacy and increasing the environmental risk of pesticide [6].

Most pesticide compounds are insoluble in aqueous media, which obstruct the development of environment friendly formulations and their efficient application [2, 7]. According to the Ostwald-Freundlich equation, when all the other factors are fixed, the solubility of substance increases as the particle size reduces. Therefore, decreasing particle size of pesticide could effectively enhance its dissolution performance [8–10]. However, obvious change appears only when the particle size is in the nanoscale. Nanotechnology may become an innovative strategy to produce nanoformulations for increasing the solubility and efficacy of insoluble pesticides [11, 12].

Emamectin benzoate, a macrocyclic lactone biological insecticide (Figure 1), is a new type of high efficient semisynthetic derivative antibiotic insecticide produced from the fermentation product of avermectin B_1. It has a broad spectrum, ultra-high efficiency, low toxicity, residue and environmental pollution, and improved thermal stability compared to avermectin [13–16]. Compared with avermectin, the insecticidal activity is increased by 1–3 orders of magnitude. It is extremely active to the lepidoptera insect larvae and many other pests and mites. At the same time, it is not harmful to the beneficial insects and benefits the comprehensive control

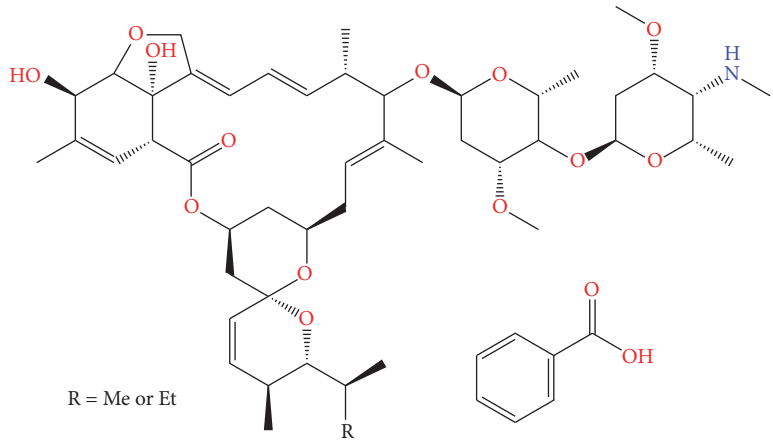


Figure 1: Chemical structure of emamectin benzoate.

of pests [17]. Owing to its low water solubility (24 mg/L^{-1}), the currently primary formulations of emamectin benzoate are still EC with numerous organic solvents and WDG with lots of surfactants. However, the organic solvent dosage of most EC is usually over 80% [18], which increased environmental pollution [19–21]. In recent years, 5.7% emamectin benzoate WDG developed rapidly [22]. However, relative to the low content of emamectin benzoate, the high concentrated surfactants with several times of pesticide in WDG also increase the ecological risk [23–28]. Although the nanoformulations have the potential for avoiding organic solvents, reducing surfactants, and enhancing water solubility of poorly water-soluble pesticide, few researches were reported, especially the solid nanodispersions.

In this research, emamectin benzoate solid nanodispersion (SND) was prepared with the method of solidifying the nanoemulsion. The solid nanoformulation presented great stability, dispersibility, wettability, spreadability, and biological activity. Moreover, the surfactant content in the composition was only 1.3 times that of pesticide which was much lower than most other solid formulations. This research supplies an innovative method to develop a solid nanoformulation with enhanced environmental compatibility and safety and may become a promising alternative for conventional formulations.

2. Experimental Methods

2.1. Materials. Emamectin benzoate (75%) was purchased from Hebei Veyong Bio-Chemical Co., Ltd., China. Ethyl acetate was provided by Beijing Jinhui Reagent Chemical Co., Ltd., China. Silwet 408# was purchased from Cangzhou Hongyuan Agrochemical Co., Ltd., China. Polyoxyethylene sorbitan monooleate (Tween 80#) was purchased from J&K Scientific Ltd., China. Two emamectin benzoate microemulsions were purchased from Shenzhen Noposion Agrochemical Co., Ltd., China (5.7%, ME-A), and Shanxi Royal Crop Science and Technology Co., Ltd., China (5.7%, ME-B), respectively. Three emamectin benzoate water dispersible granules were purchased from Shanxi Sunger Road Bio-Science Co., Ltd., China (5.7%, WDG-A), Qingdao Star Cropscience Co., Ltd., China (5.7%, WDG-B), and Shanxi Hentian Chem-Tech Co., Ltd., China (5.7%, WDG-C), respectively. High performance liquid chromatography (HPLC) grade acetonitrile, methanol, and ammonium acetate were purchased from Thermo Fisher Scientific Co., Ltd., China. Milli-Q water (18.2 MΩ·cm, TOC ≤ 4 ppb) was used in all analytical experiments.

2.2. Preparation of Emamectin Benzoate Solid Nanodispersion. Emamectin benzoate solid nanodispersion was produced by solidifying nanoemulsion method. The preparation process of the 15.0% emamectin benzoate solid nanodispersion was described in detail as follows. First of all, 5.00 g emamectin benzoate technical material (TC) powder was dispersed in 13.00 mL ethyl acetate while stirring until transparent, as an oil phase. The surfactants of 2.50 g Silwet 408# and 2.50 g Tween 80# (1/1, w/w) were dissolved in 72.00 mL deionized water and stirred until transparent; then 7.00 mL ethyl acetate was added dropwise and stirred until transparent, to get the water phase. After that, the oil phase was added to the water phase gradually and stirred. Subsequently, a carrier solution of 15.00 g sucrose and 15.00 g deionized water (1/1, w/w) was mixed with the above mixture. Finally, after stirring evenly, the mixture was freeze-dried in dark using a freeze dryer (FD-81, Tokyo Rikakikai Co., Ltd., Japan) for 60 h at 0.4 Pa to obtain the emamectin benzoate solid nanodispersion.

2.3. Particle Size and Zeta Potential of Emamectin Benzoate Solid Nanodispersion. The mean particle size, polydispersity index (PDI), and zeta potential of the redispersed aqueous emulsion were measured by dynamic light scattering (DLS) using a Zetasizer Nano Instrument (ZS90, Malvern Instruments Ltd., Worcestershire, UK) at room temperature. Mean particle size was expressed by the mean size and 50% and 90% diameter percentile (Di50 and Di90). PDI values smaller than 0.5 imply a very narrow size distribution. Zeta potential values above an absolute value of 30 mV imply that the

suspension has fine stability. The measurement was carried out in triplicate for reliability.

2.4. Morphology Characterization of the Nanoparticles. The morphology of emamectin benzoate solid nanodispersion was characterized by a JSM-7401F scanning electron microscopy (SEM) (JEOL Ltd., Japan) with an accelerating voltage of 3 kV. In the SEM image, the emamectin benzoate solid nanodispersion aqueous dispersion was prepared and imaged. After the solidifying process, the sample was configured as a solution in deionized water and centrifuged at 10,000 rpm for 20 minutes, and the supernatant was removed and then diluted with deionized water to observe the small nanoparticles. The samples were dropped on cleaned silicon slice, dried naturally, and coated with a thin layer of platinum for 30 s using a sputter coater (ETD-800, Beijing Elaborate Technology Development Co., Ltd., China).

2.5. Crystallinity Characterization of the Nanoparticles. The crystalline state of emamectin benzoate solid nanoparticles was characterized by an X-ray diffractometer (D8 Advance, Bruker AXS Inc., Germany) with Cu Kα radiation generated at 40 kV voltage and 40 mA current. Samples were analyzed in a 2θ range of 5–50°, with a step size of 0.02° and a time step of 0.1 s.

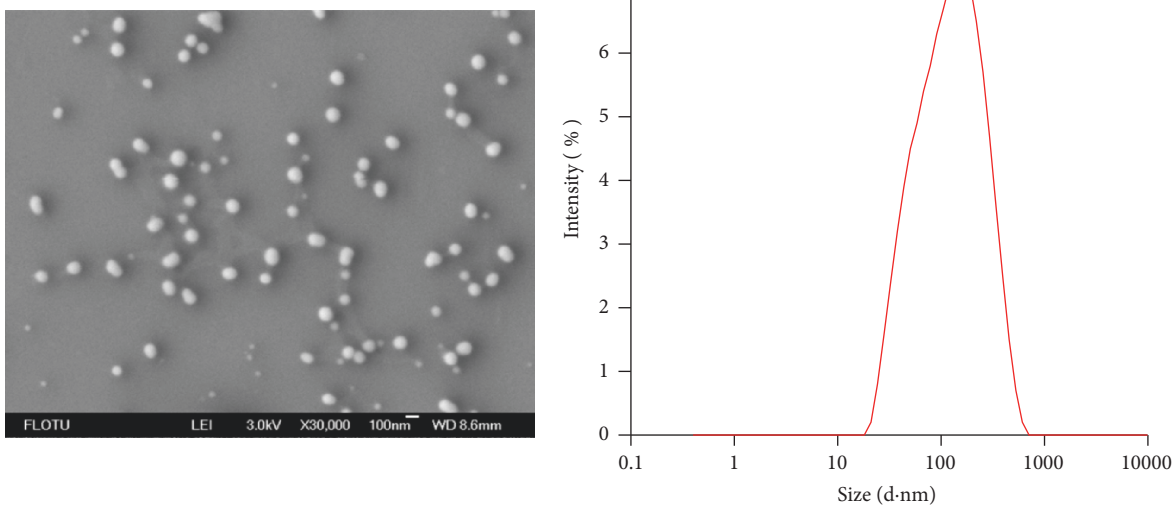
2.6. Content Determination of Emamectin Benzoate Solid Nanodispersion. The emamectin benzoate content was analyzed by HPLC (Waters 035876, Waters Alliance Co., Ltd., Milford, MA, USA) at 25°C using a C18 analytical column (5 um, 4.6 mm ∗ 250 mm, Shiseido Company, Limited, Japan) and 245 nm UV detector. The mobile phase was a mixture of acetonitrile, methanol, and 0.02% aqueous ammonium acetate (40 : 40 : 20, v/v) and the flow rate was 1.0 mL/min.

2.7. Storage Stability Measurement of Emamectin Benzoate Solid Nanodispersion. The storage stability was examined as the following instructions. The solid nanodispersions were stored in a closed dark glass bottle at 4°C, 25°C, and 54°C for 14 days. During and after storage, samples were drawn to determine the physical and chemical stability at 0 day, 2 days, 4 days, 6 days, 8 days, 10 days, 12 days, and 14 days, respectively. Physical stability was evaluated by analyzing emamectin benzoate mean particle size, Di90, and PDI with DLS. Chemical stability was measured by analyzing emamectin benzoate remaining of the solid nanodispersions with HPLC.

2.8. Contact Angle Measurement of Emamectin Benzoate Solid Nanodispersion. The contact angles of the samples on cabbage and cucumber leaves were measured using a precision contact angle measuring instrument (JC2000D2M, Shanghai Zhongchen Digital Technic Apparatus Co., Ltd., China). The specific operations were as follows: the fresh plant leaves were collected and smoothly fixed on the stage, while keeping the foliage in a natural state without destroying their structure. The liquid to be tested was drawn using a microinjector, and then 5 mL liquid droplets were injected out on the target leaf surfaces, 30 s later, the droplets were captured with a contact angle measuring instrument, and the contact angles of the droplets were calculated by 5-point fitting analysis method at (25 ± 2)°C and the relative humidity was (25 ± 2)%. Five samples were tested and averaged for each sample.

2.9. Retention Test of Emamectin Benzoate Solid Nanodispersion. Retention was determined using an impregnation method. First of all, the emamectin benzoate solid nanodispersion and commercial samples were diluted into aqueous dispersions containing 0.020 mg/mL active ingredient. Then the weight of each solution was weighed using an electronic balance (Me204e, Mettler Toledo, Zurich, Switzerland), and the area of each plant leaf was measured by a leaf area meter (Yaxin-1241, Beijing Yaxin Science Instrument Technology Co., Ltd., Beijing, China). Afterwards, the leaves were fully immersed in the above dispersions and pure water which was as a control test and then pulled out after 10 s. The weight of the aqueous dispersions was recorded before and after immersing when there were no droplets falling from the leaf surface. The weights and areas were accurate to 1 mg and 0.1 cm^2, respectively. The average value of five examinations was adopted.

2.10. Bioassays of Emamectin Benzoate Solid Nanodispersion. Biological toxicity assays were conducted using the spray method and performed according to NY/T 1154.9-2008 (Guideline for laboratory bioassay of pesticides-Part 9: Spraying method, China) [29]. The experimental procedure is as follows: on the basis of pretest, each agent sample was directly diluted with pure water into different concentrations according to the equal ratio, followed by ultrasound with an ultrasonic machine (Kq-500de, Kunshan Ultrasonic Instruments Co., Ltd., Jiangsu, China) for 5 minutes, to obtain the dispersions with different emamectin benzoate concentrations. Subsequently, the leaves of the test plants, which had not been exposed to the chemicals, were air-dried after being washed in water and cut into appropriate size and then placed in a φ6.0 cm moistened culture dish with a wet filter paper at the bottom. Afterwards, twenty healthy test insects were gently introduced into per dish with a brush and sprayed accurately in a potter sprayer (Burkard Manufacturing Co. Ltd., UK) (at a spray pressure of 100 kPa with a spray volume of 3 mL per treatment and sedimentation time of 30 s) and then sealed with plastic wrap and played about 20 breathable holes on the plastic membrane with entomic needle. Four replications were carried out for comparison with the blank control test in which leaves were only treated with deionized water solution. The treated larvae were housed in the pest control room under the conditions of light/dark = 16 : 8, temperature = (25 ± 2)°C and relative humidity = (75 ± 5)%. Test insects mortality was assessed after treatment for 48 h. The numbers of dead and live insects were examined, respectively, under the dissecting microscope (SZ61, Olympus Corporation, Japan). The insects with feet and tentacles trembling were regarded as live.



(a) (b)

Figure 2: (a) SEM image of emamectin benzoate nanoparticles and (b) particle size distribution of emamectin benzoate SNDs measured by DLS.

2.11. Statistical Analysis. The particle sizes data were recorded as the mean ± standard deviation (SD). Statistical analysis was performed with the software package SPSS (International Business Machines Corporation, New York, USA). The concentration-mortality data such as toxicity regression equation, correlation coefficient, and median lethal concentration (LC_{50}, g/mL) and their 95% confidence limit were calculated by DPS statistical software (Refine Information Tech. Co., Ltd., Hangzhou, China).

3. Results and Discussion

3.1. Particle Size and Zeta Potential of Emamectin Benzoate Solid Nanodispersion. The emamectin benzoate content in the solid nanodispersion prepared by the solidifying nanoemulsion method was 15.0%; this content was higher than the market 5.7% ME and WDG. In addition, the content of surfactants was 20.0% in the nanoformulation, which only 1.3 times of the emamectin benzoate weight. Generally, the surfactants in the conventional formulation compositions include anionic surfactants, cationic surfactants, amphoteric surfactants, nonionic surfactants, and mixed surfactants [30–36]. In the conventional formulations, the content of surfactants and cosurfactants is generally 10–20 times of emamectin benzoate weight, and the content of organic solvents and cosolvents is generally 10–30 times of emamectin benzoate weight [20, 37–49]. Relative to commercial ME and nanoemulsion, the SND has little surfactants and lacks solvents. However, its diluted aqueous solution presents the properties of ME and nanoemulsion. The results of DLS measurement show that the mean particle size, Di50, Di90, and PDI of the solid nanodispersion were 96.6 ± 1.7 nm, 126.0±3.5 nm, 300.3±25.7 nm, and 0.352±0.041, respectively, indicating an excellent redispersibility. The zeta potential value of the redispersed nanoemulsion was 31.3 ± 0.5 mV. This high zeta potential suggested the excellent physical stability [50–52]. As reported, the solid microemulsions of emamectin benzoate with the same content of surfactants were prepared by a self-emulsifying method; their emamectin benzoate concentration can reach 3.5% (w/w) [53]. In this solid nanodispersion produced by the solidifying nanoemulsion method, the emamectin benzoate content could be higher than the reported solid microemulsions.

3.2. Morphology of Emamectin Benzoate Nanoparticles. In the SEM image, the pesticide nanoparticles presented sphere shape as observed in Figure 2(a). The particle size was about 100 nm, which was well in agreement with the result measured using DLS (Figure 2(b)).

3.3. Crystalline State Analysis. As shown in Figure 3, XRD pattern of the solid nanodispersion presented the amorphous characteristic compared to the pure emamectin benzoate nanocrystal, owing to the amorphous surfactants covering the pesticide surface. The intense peaks of the solid nanodispersion mainly resulted from sucrose crystal which accounted for the largest proportion in the formulation composition. In addition, the characteristic peaks of pure emamectin benzoate at 11.8°, 19.0°, 19.7°, 22.2°, and 24.9° observed in the pattern indicated the preservation of pesticide crystal structure. The crystalline state was stable during storage and the amorphous component could accelerate the dissolution of poorly water-soluble compound [54–56]. Moreover, the zeta potential value of 31.3 ± 0.5 mV suggested the high electrostatic repulsion between the nanoparticles, contributing to the great storage stability.

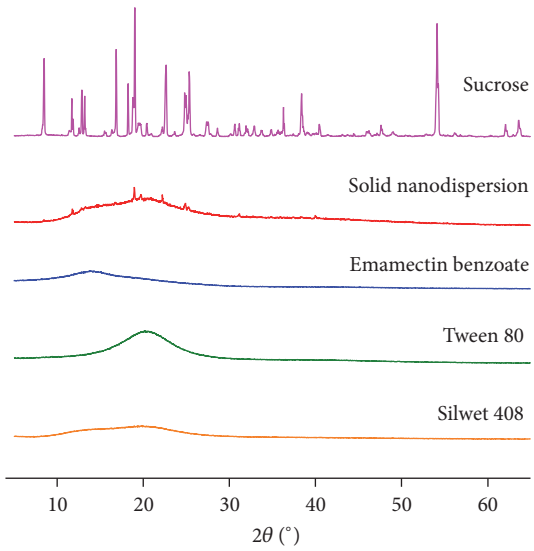


Figure 3: XRD patterns of the emamectin benzoate solid nanodispersion and pure components in the formulation.

3.4. Storage Stability. Changes of particle size and distribution of the emamectin benzoate solid nanodispersion during storage at 4°C, 25°C, and 54°C are shown in Figure 4. The mean size of nanoparticles increased from 101.4 nm to 128.2 nm, 128.2 nm, and 380.4 nm at 4°C, 25°C, and 54°C after 14 days of storage, respectively (Figure 4(a)). Particularly, the particle size and the PDI still kept at about 124.1 nm and 0.449 after 70 days of storage at 4°C. It can be seen that the changes of particle size at 4°C and room temperature were slight. This slight aggregation phenomenon is difficult to avoid, especially for nanoparticles [57–59]. In the heat storage condition, because the two surfactants (Silwet 408# and Tween 80#) are liquid at room temperature, high temperature will accelerate the mobility of additives and led to the aggregation. However, the redispersed nanoemulsion also presented colorless and transparent appearance. From the analysis of HPLC results, the contents of emamectin benzoate in the nanoformulation after 14 days of storage at 4°C, 25°C, and 54°C were 14.8%, 14.7%, and 14.7%, respectively, almost no change at all (Figure 4(b)). These results suggested the excellent physical and chemical stability of emamectin benzoate solid nanodispersion.

3.5. Contact Angle of Emamectin Benzoate Solid Nanodispersion. The contact angle was the important index to evaluate the wettability of the solution. Cabbage leaves were used as the typical hydrophobic interface, cucumber leaves as a typical hydrophilic interface. Commercial MEs and WDGs were used as the control formulations. The wettability effect of emamectin benzoate SND was studied. As shown in Figure 5, the contact angle of the emamectin benzoate SND on the surface of cabbage leaves was 98°, smaller than the ME-B, WDG-A, WDG-B, and WDG-C, indicating that the SND has better infiltration at the hydrophobic plant leaf interface. The contact angle of the SND on cucumber leaves was 49°, which was less than that of the ME-A, ME-B, WDG-A, WDG-B, and WDG-C, indicating a significant increase in the wettability. The contact angle reflects the wetting and spreading properties of the liquid on the target surface. The smaller contact angle implies better wetting and spreading performance [60]. When the wettability of the SND on the hydrophobic cabbage and rice was better than that of the control ME and WDG formulations, it was favorable for the attachment and distribution of the insoluble drug-loaded particles on the foliage, enhancing the adhesion on the target and efficacy.

3.6. Retention Test. Retention affects the pesticide efficacy via influencing spread and adhesion of aqueous dispersions on leaves after spraying. The retention (R_m, mg/cm^2) was evaluated by the improved method of previous literature [61] and evaluated by the following equation:

$$R_m = \frac{W_0 - W_1}{S}. \quad (1)$$

Here, W_0 (mg) and W_1 (mg) are the weights of the test aqueous solutions before and after immersing the hydrophobic rice *(Oryza sativa L.)*, cabbage *(Brassica oleracea* L.*)* leaves, and hydrophilic cucumber *(Cucumis sativus Linn)* leaves; S (cm^2) is the area of the leaves. As shown in Figure 6, the retention of the emamectin benzoate solid nanodispersion on the hydrophobic rice leaves was 0.89, 1.00, 3.17, 3.12, 3.32, and 4.77 times that of commercial ME-A, ME-B, WDG-A, WDG-B, WDG-C, and deionized water, respectively. The retention of the emamectin benzoate solid nanodispersion on the hydrophobic cabbage leaves was 1.11, 1.12, 1.27, 1.31, 1.33, and 1.76 times that of commercial ME-A, ME-B, WDG-A, WDG-B, WDG-C, and pure water, respectively. The commercial MEs had good retention due to the addition of a large amount of surfactant and solvent, but the SND retention was increased due to the small particle size and large specific surface area. The above results suggest that while the particle size reduces, their specific surface area and contact area with leaves increase, which is beneficial to expanding the retention of pesticides. The retention of the emamectin benzoate solid nanodispersion on the cucumber rice was 1.04, 1.05, 1.04, 1.00, 1.05, and 1.04 times that of commercial ME-A, ME-B, WDG-A, WDG-B, WDG-C, and deionized water, respectively. This difference was not obvious, which may be related to the hydrophilic characteristic of cucumber leaves.

3.7. Biological Activity. The biological activities of emamectin benzoate SND, MEs, and WDGs against diamondback moths *(Plutella xylostella* L.*)* and green peach aphid *(Myzus persicae (Sulzer))* were compared in Tables 1 and 2. Table 1 result showed that the median lethal concentration (LC_{50}) of ME-B, WDG-A, WDG-B, and WDG-C against diamondback moths was 1.24, 1.45, 1.81, and 1.87 times of SND, respectively, indicating SND having higher sensitivity. Therefore, the toxicities of these agents against diamondback moths were SND > ME-B > WDG-A > WDG-B > WDG-C. Table 2 data showed that the toxicities of WDG-A and WDG-B were significantly lower than that of SND; their LC_{50} were 2.14- and 2.65-folds of SND, respectively. From the above analysis, the toxicities

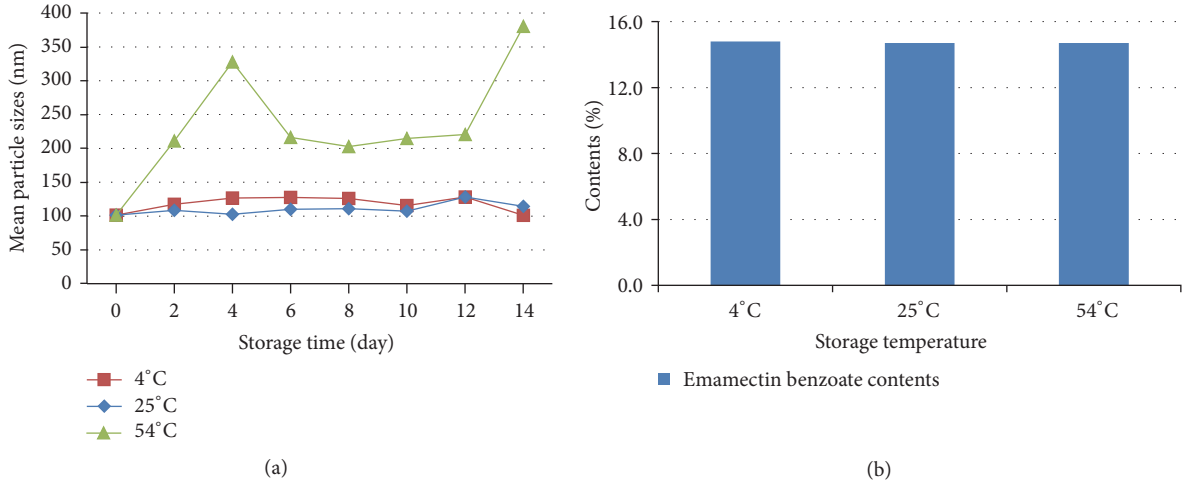


Figure 4: Storage stability of emamectin benzoate solid nanodispersion. (a) Physical stability and (b) chemical stability.

Table 1: Bioassay results of emamectin benzoate formulations against diamondback moths.

Formulation	Toxicity regression equation	Correlation coefficient	LC_{50} (μg/mL)	95% confidence limit (μg/mL)
SND	$Y = 5.6862 + 0.9328x$	0.9871	0.1838	0.1142–0.2960
ME-A	$Y = 6.1144 + 1.1443x$	0.9942	0.1062	0.0725–0.1557
ME-B	$Y = 6.7321 + 2.6898x$	0.9257	0.2270	0.0661–0.7802
WDG-A	$Y = 6.6717 + 2.9105x$	0.8708	0.2667	0.0616–1.1527
WDG-B	$Y = 6.1196 + 2.3456x$	0.9467	0.3332	0.1320–0.8412
WDG-C	$Y = 6.1191 + 2.4146x$	0.9285	0.3440	0.0958–1.2354

Table 2: Bioassay results of emamectin benzoate formulations against green peach aphid.

Formulation	Toxicity regression equation	Correlation coefficient	LC_{50} (μg/mL)	95% confidence limit (μg/mL)
SND	$Y = 1.4958 + 1.4428x$	0.9924	268.3323	150.3596–907.6823
WDG-A	$Y = 2.5995 + 0.8698x$	0.9461	575.3891	233.3131–5373.9177
WDG-B	$Y = 3.3398 + 0.5822x$	0.8826	710.7140	228.6222–30344.20774

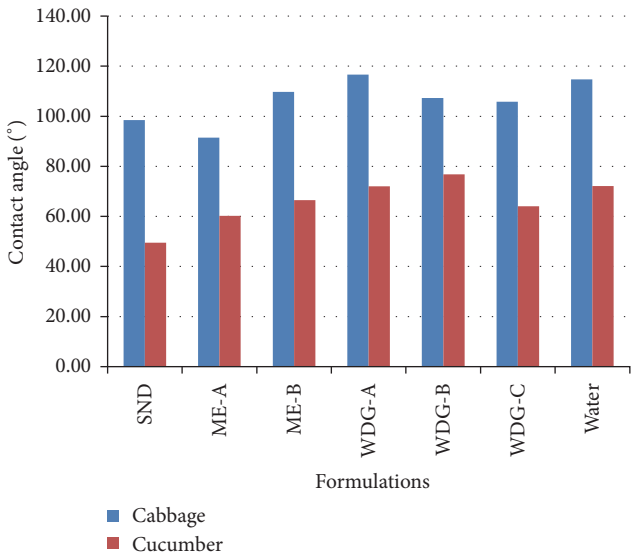


Figure 5: Contact angle of emamectin benzoate on cabbage and cucumber leaf surface.

effect of three agents against green peach aphid was SND > WDG-A > WDG-B. As reported, the efficacy strengthened as the droplet size of pesticide reduced. The above results were consistent with literature [62, 63]. Nanopesticides could be more potent than conventional pesticide formulations against harmful target organisms, due to their larger specific surface area which could increase the adsorption and accumulation of the active ingredient by the pest [64, 65].

4. Conclusion

In summary, the solid nanodispersion of 15% (w/w) emamectin benzoate containing 20% surfactants (w/w) with high dispersity and stability was prepared by the solidifying nanoemulsion method. It was evidenced that the surfactants had big influence on the particle size and dispersity of the solid nanodispersion. The emulsifier combination of two nonionic surfactants (Silwet 408# and Tween 80#, 1/1, w/w) had superior emulsifying properties, and the content 1.3 times of pesticide was enough to show excellent nanoemulsifying

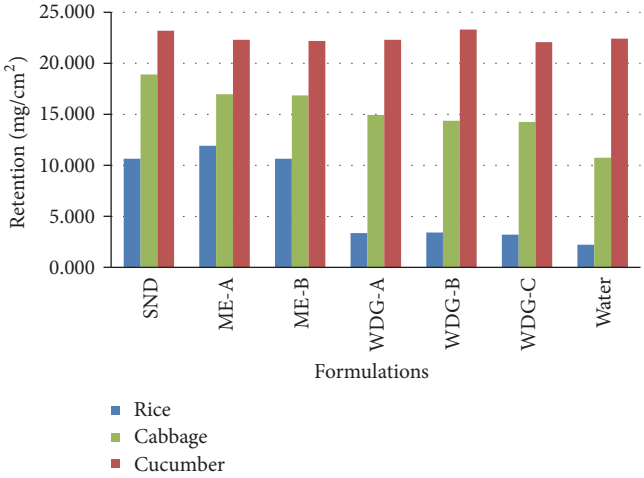


FIGURE 6: Retention of emamectin benzoate SND, MEs, WDGs, and deionized water on leaves.

feature. The solid nanodispersion changed into aqueous nanoemulsion after redispersing it with deionized water. The mean particle size and zeta potential value of the redispersed nanoemulsion were 96.6 ± 1.7 nm and 31.3 ± 0.5 mV, respectively. Its small particle size, high zeta potential, and stable crystalline state suggested the super dispersed uniformly and excellent storage stability. Moreover, the solid nanodispersion reduced the leaf contact angle, increased the retention and biological activity compared to conventional solid formulations. The composition of solid nanodispersion increases the content of emamectin benzoate, avoids organic solvents, and reduces surfactants compared with EC, ME, and WDG. Therefore, this research offers a simplified and universal method to produce solid nanoformulation and this kind of nanoformulation is perspective in plant and environment protection for improving bioavailability and ecological security.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Dongsheng Yang and Bo Cui contributed equally to this work.

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References

[1] P. K. Jensen and M. H. Olesen, "Spray mass balance in pesticide application: A review," *Crop Protection*, vol. 61, pp. 23–31, 2014.

[2] B. S. Sekhon, "Nanotechnology in agri-food production: an overview," *Nanotechnology, Science and Applications*, vol. 7, no. 2, pp. 31–53, 2014.

[3] A. P. Pratap and D. N. Bhowmick, "Pesticides as microemulsion formulations," *Journal of Dispersion Science and Technology*, vol. 29, no. 9, pp. 1325–1330, 2008.

[4] L. Qian and T. Li, "Review of reproductive toxicity of environmental chemical pollutants," *Journal of Environmental and Occupational Medicine*, vol. 22, no. 2, pp. 167–171, 2005.

[5] L. Chen, X. Yu, J. Chen, Q. Ye, and H. Fang, "Preliminary application of new formulation of pesticides in safety production of Jiaobai," *Acta Agriculturae Zhejiangensis*, vol. 15, no. 3, pp. 177–180, 2003.

[6] A. Knowles, "Recent developments of safer formulations of agrochemicals," *Environmentalist*, vol. 28, no. 1, pp. 35–44, 2008.

[7] L. Yang, "Problems and development trend of avermectins pesticide formulations," *World Pesticides*, vol. 31, pp. 5–7, 2009.

[8] A. Mihranyan and M. Strømme, "Solubility of fractal nanoparticles," *Surface Science*, vol. 601, no. 2, pp. 315–319, 2007.

[9] S. M. Dizaj, Z. Vazifehasl, S. Salatin, K. Adibkia, and Y. Javadzadeh, "Nanosizing of drugs: effect on dissolution rate," *Research in Pharmaceutical Sciences*, vol. 10, no. 2, pp. 95–108, 2014.

[10] S. B. Murdande, D. A. Shah, and R. H. Dave, "Impact of nanosizing on solubility and dissolution rate of poorly soluble pharmaceuticals," *Journal of Pharmaceutical Sciences*, vol. 104, no. 6, pp. 2094–2102, 2015.

[11] I. Ishaaya, R. Nauen, and A. R. Horowitz, *Insecticides Design Using Advanced Technologies*, Springer Science & Business Media, 2007.

[12] Y. Sasson, G. Levy-Ruso, O. Toledano et al., "Nanosuspensions: emerging novel agrochemical formulations," in *Insecticides Design Using Advanced Technologies*, pp. 1–39, Springer, Berlin, Germany, 2009.

[13] L. Zhou, F. Luo, X. Zhang, Y. Jiang, Z. Lou, and Z. Chen, "Dissipation, transfer and safety evaluation of emamectin benzoate in tea," *Food Chemistry*, vol. 202, pp. 199–204, 2016.

[14] P. J. Han, R. J. Fan, Y. T. Feng, E. Q. Du, and R. H. Zhao, "Control efficacy of 2.2% emamectin benzoate ME against rice stem borer (Chilo suppressalis)," *Journal of Southern Agriculture*, vol. 42, no. 4, pp. 403–405, 2011.

[15] Q. Shang, Y. Shi, Y. Zhang, T. Zheng, and H. Shi, "Pesticide-conjugated polyacrylate nanoparticles: novel opportunities for improving the photostability of emamectin benzoate," *Polymers for Advanced Technologies*, vol. 24, no. 2, pp. 137–143, 2013.

[16] M. Guo, W. Zhang, G. Ding et al., "Preparation and characterization of enzyme-responsive emamectin benzoate microcapsules based on a copolymer matrix of silica-epichlorohydrin-carboxymethylcellulose," *RSC Advances*, vol. 5, no. 113, pp. 93170–93179, 2015.

[17] J. P. Ni, H. M. Hou, X. Zeng, and C. X. Huang, "Bioactivity comparison on emamectin-benzoate and avermectin , modern agrochemicals," *Modern Agrochemicals*, vol. 2, no. 3, pp. 38–40, 2003.

[18] F. L. Chen, "Present situation and development trend of EC products in China," *Symposium on Environmentally-Friendly Pesticide Emulsion Development*, pp. 40–47, 2011.

[19] L. Y. Liu, "HPLC Analysis of 0.2% Hypertonic Emamectin-benzoate EC," *Modern Agrochemicals*, vol. 6, no. 3, pp. 25-26, 2007.

[20] C. H. Zheng, "Development of a 1.0% emamectin benzoate microemulsion," *Anhui Chemical Industry*, vol. 38, no. 3, pp. 49–51, 2012.

[21] X. P. Yang, W. S. Lu, and Z. G. Jiang, "The Application of emamectin benzoate 1.5% EC for control of plutella xylostella and laphygma exigua hubner," *Pesticide Science and Administration*, vol. 27, no. 5, pp. 25-26, 2006.

[22] C. Q. Sun, Y. J. Wang, C. H. Zhang et al., "Effect of different disintegrants on disintegrating properties of emamectin benzoate 5.7% WG," *Pesticide Science and Administration*, vol. 34, no. 11, pp. 14–17, 2013.

[23] T. K. Fang, B. H. Cao, G. S. Yuan et al., "Study on the 5.7% wide (emamectin benzoate) water dispersible granule field control effect of rice leaf roller," *Modern Agricultural Science and Technology*, vol. 9, 134 pages, 2013.

[24] C. H. Zheng, "Development of Enamectin Benzoate 7.5% WDG," *Anhui Chemical Industry*, vol. 39, no. 4, pp. 62–64, 2013.

[25] W. Huang and Y. Zhang, "Study on the efficacy of 5.7% emamectin benzoate water–dispersible granules in controlling cotton helicoverpa armigera," *Modern Agricultural Science and Technology*, no. 6, pp. 118–122, 2013.

[26] X. J. Zhang, E. T. Li, L. Chen et al., "A dimension salt spray granulation water dispersible granule formula and process technology and industrial production problems," in *Proceedings of the Third Workshop on Processing Technology and Equipment for Environmentally Friendly Pesticide Preparations*, pp. 135–141, 2012.

[27] Z. W. Gao, H. Y. Ma, W. K. Li et al., "Preparation of Emamectin Benzoate 5% WG," *Pesticide Science and Administration*, vol. 27, no. 1, pp. 32–34, 2006.

[28] D. P. Wang and Y. Zhao, "Preparation of emamectin benzoate 5%WG," *Pesticide Science and Administration*, vol. 31, no. 3, pp. 29–32, 2010.

[29] "Guideline for laboratory bioassay of pesticides-Part 9: Spraying method," Ministry of Agriculture of the People's Republic of China, Beijing, China, NY/T 1154.9-2008.

[30] S. Ketsarin, S. Yanawath, and S. Supalax, "Study on the effect of chain-length compatibility of mixed anionic–cationic surfactants on the cloud-point extraction of selected organophosphorus pesticides," *Analytical and Bioanalytical Chemistry*, vol. 404, no. 5, pp. 1539–1548, 2012.

[31] G. Zheng, Z. Zhao, and J. W. C. Wong, "Role of non-ionic surfactants and plant oils on the solubilization of organochlorine pesticides by oil-in-water microemulsions," *Environmental Technology*, vol. 32, no. 3, pp. 269–279, 2011.

[32] J. Vichapong and R. Burakham, "Novel ultrasound-assisted mixed anionic-cationic surfactant-enhanced emulsification microextraction combined with HPLC for the determination of carbamate pesticides," *Analytical Methods*, vol. 4, no. 7, pp. 2101–2108, 2012.

[33] M. Aguilar, A. Farran, C. Serra, M. J. Sepaniak, and K. W. Whitaker, "Use of different surfactants (sodium dodecyl sulfate, bile salts and ionic polymers) in micellar electrokinetic capillary chromatography application to the separation of organophosphorus pesticides," *Journal of Chromatography A*, vol. 778, no. 1, pp. 201–205, 1997.

[34] A. Piscureanu, T. Pop, M. Dogaru, M. Piscureanu, and D. Manaila-Maximean, "Influence of non-ionic surfactants on surface activity of pesticide colloidal systems," *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, vol. 178, no. 1–3, pp. 129–133, 2001.

[35] T. Cserháti and E. Forgács, "Separation and quantitative determination of non-ionic surfactants used as pesticide additives," *Journal of Chromatography A*, vol. 774, no. 1-2, pp. 265–279, 1997.

[36] P. Yang, "Research on formulation of 25% trinexapac-ethly EC," *Guangdong Chemical Industry*, no. 2, pp. 18-19, 2013.

[37] Y. Zhang and J. H. Song, "Study on the 1% emamectin benzoate micro-emulsion," *Journal of Anhui Agricultural Sciences*, vol. 37, no. 18, pp. 8576–8578, 8677, 2009.

[38] P. Fan, Z. Y. Gu, D. J. Xu et al., "Studies on ME of emamection-benzoate which enhanced wetting and spreading performance on rice leaf," *Jiangsu Journal of Agricultural Sciences*, vol. 25, no. 5, pp. 1019–1024, 2009.

[39] Z. Y. Sun, R. N. Lin, Q. X. Fan et al., "Formulation of 1% emamection benaoate microemulsion," *Journal of Fujian Agricultural and Forestry University (Natural Science edition)*, vol. 39, no. 2, pp. 128–131, 2010.

[40] P. Fan, "Preparation of Emamectin Benzoate Microemulsion and Its Distribution in Cabbage and Rice Leaves," Yangzhou University, 2010.

[41] Z. Y. Sun, "Study on Processing and Mechanism of Emamectin Benzoate Microemulsion," Fujian Agriculture and Forestry University, 2008.

[42] J. P. Yu, "Preparation of emamectin benzoate microemulsion," in *Proceedings of the annual meeting of Pesticide Committee of China Chemical Industry Association*, pp. 315-316, 2002.

[43] J. H. Yang and R. Y. Zhao, "Study on Microemulsion of 0.5% Emamection-benzoate," *Journal of Anhui Agricultural Sciences*, vol. 34, no. 10, pp. 2190–2197, 2006.

[44] Y. P. Shao, M. Y. Chen, L. X. Hao et al., "Research of preparation of suspension concentration of 6% AvermectinsBla benzoate and it's field efficacy," *Pesticide Science and Administration*, vol. 33, no. 2, pp. 16–19, 2012.

[45] J. H. An, "Study of emamectin Micor-Emulsion," *Hebei Chemical Engineering and Industry*, vol. 32, no. 8, pp. 12–13, 38, 2009.

[46] X. D. Wen, "Recipe optimization and field efficacy trials of emamectin benzoate," *China Fruit Avegetable*, no. 8, pp. 45–47, 2015.

[47] Z. Y. Hong and S. H. Hong, "The application of surfactant in 2% emamectin benzoate microemulsion," *China Surface Active Agents*, pp. 241–244, 2007.

[48] Y. P. Wang and Y. W. Wang, "Preparation of 0.5% emamectin benzoate microemulsion and its field efficacy test," in *Proceedings of the Second National Symposium on New Technologies and Products for Green Pesticides*, pp. 220–225, 2003.

[49] M. M. Jia, "Preparation of nano–avermectin benzoate–HPlc nano–controlled release system," *Shandong Agricultural University*, 2011.

[50] N. S. Souza, A. D. Rodrigues, C. A. Cardoso et al., "Physical properties of nanofluid suspension of ferromagnetic graphite with high Zeta potential," *Physics Letters, Section A: General, Atomic and Solid State Physics*, vol. 376, no. 4, pp. 544–546, 2012.

[51] A. B. Kovačević, R. H. Müller, S. D. Savić, G. M. Vuleta, and C. M. Keck, "Solid lipid nanoparticles (SLN) stabilized with polyhydroxy surfactants: preparation, characterization and physical stability investigation," *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, vol. 444, pp. 15–25, 2014.

[52] J. Das Neves, M. Amiji, M. F. Bahia, and B. Sarmento, "Bruno assessing the physical-chemical properties and stability of dapivirine-loaded polymeric nanoparticles," *International Journal of Pharmaceutics*, vol. 456, no. 2, pp. 307–314, 2013.

[53] L. Feng, B. Cui, D. Yang et al., "Preparation and Evaluation of Emamectin Benzoate Solid Microemulsion," *Journal of Nanomaterials*, vol. 2016, Article ID 2386938, 7 pages, 2016.

[54] C. Leuner and J. Dressman, "Improving drug solubility for oral delivery using solid dispersions," *European Journal of Pharmaceutics and Biopharmaceutics*, vol. 50, no. 1, pp. 47–60, 2000.

[55] P. Kanaujia, P. Poovizhi, W. K. Ng, and R. B. H. Tan, "Amorphous formulations for dissolution and bioavailability enhancement of poorly soluble APIs," *Powder Technology*, vol. 285, pp. 2–15, 2015.

[56] R. H. Müller, C. Jacobs, and O. Kayser, "Nanosuspensions as particulate drug formulations in therapy: rationale for development and what we can expect for the future," *Advanced Drug Delivery Reviews*, vol. 47, no. 1, pp. 3–19, 2001.

[57] P.-F. Yue, Y. Li, J. Wan, M. Yang, W.-F. Zhu, and C.-H. Wang, "Study on formability of solid nanosuspensions during nanodispersion and solidification: I. Novel role of stabilizer/drug property," *International Journal of Pharmaceutics*, vol. 454, no. 1, pp. 269–277, 2013.

[58] M. George and I. Ghosh, "Identifying the correlation between drug/stabilizer properties and critical quality attributes (CQAs) of nanosuspension formulation prepared by wet media milling technology," *European Journal of Pharmaceutical Sciences*, vol. 48, no. 1-2, pp. 142–152, 2013.

[59] S. F. Chow, K. Y. Wan, K. K. Cheng et al., "Development of highly stabilized curcumin nanoparticles by flash nanoprecipitation and lyophilization," *European Journal of Pharmaceutics and Biopharmaceutics*, vol. 94, pp. 436–449, 2015.

[60] L. Zhou, "Wettability and dynamic behavior of several pesticide surfactant solutions on different targets," Beijing: China Agricultural University, 2007.

[61] H. Z. Yuan, S. H. Qi, and D. B. Yang, "Study on the point of runoff and the maximum retention of spray liquid on crop leaves," *Chinese Journal of Pesticide Science*, vol. 2, pp. 66–71, 2000.

[62] S. Atta, M. Bera, T. Chattopadhyay et al., "Nano-pesticide formulation based on fluorescent organic photoresponsive nanoparticles: for controlled release of 2,4-D and real time monitoring of morphological changes induced by 2,4-D in plant systems," *RSC Advances*, vol. 5, no. 106, pp. 86990–86996, 2015.

[63] C. H. Anjali, Y. Sharma, A. Mukherjee, and N. Chandrasekaran, "Neem oil (*Azadirachta indica*) nanoemulsion—a potent larvicidal agent against *Culex quinquefasciatus*," *Pest Management Science*, vol. 68, no. 2, pp. 158–163, 2012.

[64] P. Saini, M. Gopal, R. Kumar, and C. Srivastava, "Development of pyridalyl nanocapsule suspension for efficient management of tomato fruit and shoot borer (Helicoverpa armigera)," *Journal of Environmental Science and Health - Part B Pesticides*, vol. 49, no. 5, pp. 344–351, 2014.

[65] C. H. Anjali, S. Sudheer Khan, K. Margulis-Goshen, S. Magdassi, A. Mukherjee, and N. Chandrasekaran, "Formulation of water-dispersible nanopermethrin for larvicidal applications," *Ecotoxicology and Environmental Safety*, vol. 73, no. 8, pp. 1932–1936, 2010.